have been amended herein. New claims 66-81 have been added. Upon entry of the present Amendment, claims 25-27, 40, 44-50, 53-64 and 66-81 will be pending.

As a preliminary matter, Applicants thank the Examiner for allowing time to interview the present application on March 20, 2001 along with Mr. Bartfeld and Mr. Straher.

As recommended in the Office Action, claim 48 has been amended to correct the inadvertent misspelling of "polycytidylic."

I. Double Patenting Rejections

Claims 1, 3, 5, 12, 13, 23, 24, 41-43 and 60-65 stand provisionally rejected under 35 U.S.C. §101 as claiming the same invention as that of claims 1-24 of co-pending application Serial No. 08/886,829. Applicants have cancelled claims 1, 3, 5, 12, 13, 23, 24, 41-43 and 65. Applicants respectfully request that this rejection, as may be applied to claims 60-64, be deferred until allowable subject matter is indicated.

Claims 25-27, 32, 33, 35-38 and 40 stand provisionally rejected under the doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-47 of co-pending application Serial No. 08/886,829. Applicants have cancelled claims 32, 33 and 35-38. Applicants respectfully request that this rejection, as may be applied to claims 25-27 and 40, also be deferred until allowable subject matter is indicated.

II. The Claimed Inventions Are Novel

A. WO 97/05903

Claims 44-46, 49, 53, 54, 56 and 57 stand rejected under 35 U.S.C. §102(a) as allegedly being unpatentable over WO 97/05903 (hereinafter, the "903 reference"). Applicants request reconsideration thereof in view of the amended claims.

The standard for anticipation under §102 is one of strict identity. An anticipation rejection requires a showing that each limitation of a claim be found in a single reference. *Atlas Powder Co. v. E.I. DuPont de Nemours & Co.*, 224 U.S.P.Q. 409, 411 (Fed. Cir. 1984). As was pointed out

during the interview, the 903 reference does not teach or suggest a nucleic acid having at least one chemical modification selected from the group consisting of a cytosine to 5-methyl-cytosine substitution, a phosphorothioate linkage, or a 2'-methoxyethoxy modification, as is recited in amended claim 44. Thus, the 903 reference does not anticipate the claimed inventions. Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. §102(a) be withdrawn.

B. U.S. Patent No. 5,707,648

Claims 44, 45, 47, 49-51, 53-55, 58 and 59 stand rejected under 35 U.S.C. §102(e) as allegedly being unpatentable over U.S. Patent No. 5,707,648 (hereinafter, the "Yiv reference"). Applicants have cancelled claim 51. Applicants request reconsideration thereof, as it may be applied to the remaining claims, in view of amended claim 44.

As was pointed out during the interview, the Yiv reference does not teach or suggest a nucleic acid having at least one chemical modification selected from the group consisting of a cytosine to 5-methyl-cytosine substitution, a phosphorothioate linkage, or a 2'-methoxyethoxy modification, as is recited in amended claim 44. Thus, the Yiv reference does not anticipate the claimed inventions. Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. §102(e) be withdrawn.

C. U.S. Patent No. 6,096,722

Claims 44-59 stand rejected under 35 U.S.C. §102(e) as allegedly being unpatentable over U.S. Patent No. 6,096,722 (hereinafter, the "Bennett reference"). Applicants have cancelled claims 51 and 52. Applicants traverse the rejection and request reconsideration thereof, as it may be applied to the remaining claims, because the Bennett reference is not prior art under §102(e).

As stated above, claim 44 has been amended to avoid the prior art of record. As was pointed out during the interview, the disclosure of an oligonucleotide in combination with two fatty acids is disclosed for the first time in the Bennett reference upon its filing date, May 27, 1998, which is after Applicants' effective filing date of July 1, 1997 for the present application. Thus, the Bennett

reference is not prior art. Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. §102(e) be withdrawn.

III. The Claims Are Clear And Definite

Claims 25-27 stand rejected under 35 U.S.C. §112, second paragraph, as allegedly being vague and indefinite. Applicants traverse the rejection and respectfully request reconsideration in view of the amended claims.

The Office Action asserts that a correlation or recapitulation step at the end of the claim which restates the preamble is missing. Applicants submit that such a step is **absolutely** not required under the patent laws. Applicants submit that MPEP §2172.01 is not meant to require Applicants to restate the preamble at the end of a method claim. Indeed, the claim is not missing elements, steps or necessary structural cooperative relationships of elements. Nor does the claim fail to interrelate essential elements of the invention as defined by Applicants in the specification. Solely in order to advance prosecution of the present application, however, Applicants have amended claim 25 to simply restate the preamble. Such amendment is not meant to be limiting in any manner. Thus, claims 25-27 are definite within the meaning of § 112. *In re Mercier*, 185 U.S.P.Q. 774 (C.C.P.A. 1975) (claims sufficiently define an invention so long as one skilled in the art can determine what subject matter is or is not within the scope of the claims). Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. §112, second paragraph, be withdrawn.

IV. The Claimed Inventions Are Enabled

Claims 1, 3, 5, 12, 13, 23-27, 32, 33, 35-38, 40-43 and 60-65 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to enable the claimed invention. Applicants have cancelled claims 1, 3, 5, 12, 13, 23, 24, 32, 33, 35-38, 41-43 and 65. The Office Action mistakenly asserts that the only utility for a pharmaceutical composition is for treatment. The Office Action also asserts that Applicants have not enabled methods of treatment or investigating the role of a gene or gene product. Applicants disagree with each of the conclusions drawn in the Office Action. The Office Action,

however, acknowledges that the specification "does provide teaching on the introduction of nucleic acids into the blood and generally into the organs of an animal via the enteral pathway." The Office Action also indicates that claims directed to methods of delivery of the compositions of claims 44-59 via the intestinal mucosa may also be enabled. Applicants traverse the rejection, as it may be applied to pending claims 25-27, 40 and 60-64 and respectfully request reconsideration because one skilled in the art would be able to practice the claimed inventions without being required to perform undue experimentation.

Applicants have amended claim 25 to recite a method of enhancing penetration of a nucleic acid across the alimentary canal of an animal comprising administering a composition of claim 44. No amount of undue experimentation is required to enhance penetration of a nucleic acid across the alimentary canal of an animal by administering a composition of claim 44. The Declaration of Dr. Hardee/Dr. Teng showed that the claimed pharmaceutical compositions, in fact, enhance penetration of a nucleic acid across the alimentary canal of an animal. Paragraphs 3-5 of the Declaration describe experiments whereby penetration of an oligonucleotide across the alimentary canal of rats and dogs is enhanced by delivery of the oligonucleotide along with at least two fatty acids. Such examples are also set forth in Applicants specification in Examples 3, 4 and 13. Thus, Applicants have clearly enabled one skilled in the art to enhance penetration of a nucleic acid across the alimentary canal of an animal by administering a pharmaceutical composition of claim 44 to the animal without requiring performance of undue experimentation. Thus, claims 25-27 are enabled by the specification.

Applicants have amended claim 40 to recite a method of modulating gene expression in a cell, a tissue, or an organism comprising administering a composition of claim 44. No amount of undue experimentation is required to modulate gene expression in a cell, tissue or organism by administering a composition of claim 44. Thus, claim 40 is enabled by the specification.

Claim 60 has been amended to recite the composition of claim 45 wherein the oligonucleotide is in prodrug form. Because claim 45 has been indicated as being enabled, amended claim 60 is also enabled.

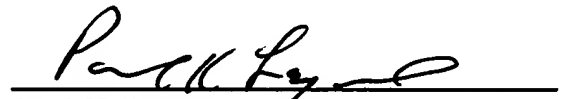
Claims 61-64 have been amended to recite a composition comprising a nucleic acid and capric acid or lauric acid. No amount of undue experimentation is required to make or use such a composition. Thus, claims 61-64 are enabled by the specification.

In view of the foregoing, Applicants respectfully request that the rejection under 35 U.S.C. §112, first paragraph, be withdrawn.

V. Conclusion

It is respectfully submitted that this application is now in condition for allowance. Accordingly, an indication of allowability and an early Notice of Allowance are respectfully requested. Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned **"Version with markings to show changes made."**

Respectfully submitted,



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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims:

Claims 1, 3, 5, 12, 13, 23, 24, 32, 33, 35-38, 41-43, 51, 52 and 65 have been cancelled.

Claims 66-81 have been added.

Claims 25, 40, 44, 48, 58, 60 and 61 have been amended as follows:

25. (Amended three times) A method of enhancing penetration of a nucleic acid across the alimentary canal of an animal comprising administering to said animal the [pharmaceutical] composition of claim [1] 44, wherein said composition enhances penetration of said nucleic acid across the alimentary canal of said animal.

40. (Amended twice) A method of modulating gene expression in a cell, a tissue, or an organism comprising administering the [pharmaceutical] composition of claim [1] 44 to said cell, tissue or organism, thereby modulating gene expression in said cell, tissue, or organism.

44. (Amended) A composition comprising a nucleic acid and at least two fatty acids or pharmaceutically acceptable salts thereof, wherein said nucleic acid has at least one chemical modification selected from the group consisting of a cytosine to 5-methyl-cytosine substitution, a phosphorothioate linkage and a 2'-methoxyethoxy modification.

48. (Amended) The composition of claim 47 wherein said carrier compound is selected from the group consisting of polyinosinic acid, dextran sulfate, [polycytidic] polycytidylic acid and 4-acetamido-4'isothiocyano-stilbene-2,2'-disulfonic acid.

58. (Amended) The composition of claim 44 further comprising a bile salt.

60. (Amended) The [pharmaceutical] composition of claim [3] 45 wherein said oligonucleotide is in prodrug form.

61. (Amended) A [pharmaceutical] composition comprising a nucleic acid and capric acid or lauric acid or a pharmaceutically acceptable salt thereof, wherein said nucleic acid has at least one chemical modification selected from the group consisting of a cytosine to 5-methyl-cytosine substitution, a phosphorothioate linkage and a 2'-methoxyethoxy modification.